

Application of the Atlas Algorithm to Identify the Carboplatin+ Gemcitabine Regimen

in Patients with Metastatic Triple-Negative Breast Cancer (mTNBC) through the French Nationwide Hospital Discharge Database (PMSI)

Introduction & objectives

Metastatic triple-negative breast cancer (mTNBC) corresponds to between 2,717 and 3,093 diagnoses in France every year according to the French National Authority for Health (HAS)¹.

Keytruda was approved in combination with chemotherapy in the treatment of locally recurrent unresectable or mTNBC in adults whose tumours express PD-L1 with a CPS $\geq$ 10 and who have not received prior chemotherapy for metastatic disease raised. This approval raised the question of the applicability of its combination with carboplatin+gemcitabine (CG), used in the KEYNOTE-355 trial, to French clinical practice².

The aim of this study was to quantify the use of the CG regimen in previously untreated locally recurrent inoperable or mTNBC patients before the approval of Keytruda in association with this protocol.

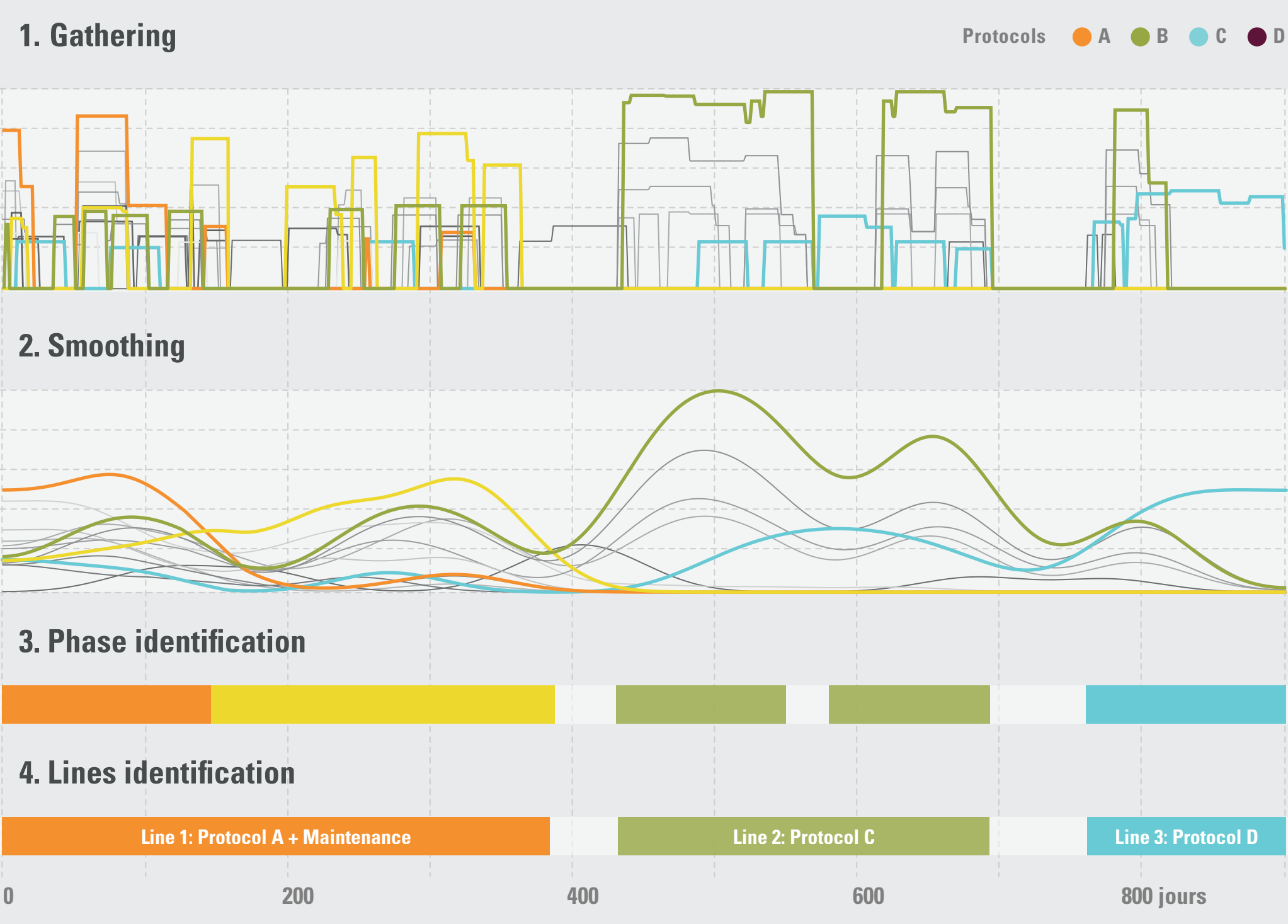
Methods

An observational retrospective study was conducted using the French exhaustive national hospital discharge database (PMSI).

All newly hospitalized (without hospitalization in the 5 preceding years) patients with metastatic (ICD-10 codes: C77, C78, C79) breast cancer (C50) between 01/01/2017 and 31/12/2020 were followed until the end of the study period (31/12/2020) or in-hospital death.

To exclude non-TNBC patients, patients without any chemotherapy session (Z51.1) and/or with administration of an anti-HER2+ treatment (Trastuzumab, Trastuzumab deruxtecan, Trastuzumab emtansine, Pertuzumab) or a treatment/procedure suggesting a HR+ status (cyclin dependent kinase 4/6 inhibitors – CDK4/6i, bilateral oophorectomy) were excluded.

Identification of ATLAS treatment lines in 4 steps for mTNBC first line treatment. For each patient: **1** calculate a similarity score with each theoretical protocol on each day of follow-up and align each of these protocols **2** Smooth the scores and identify the phases (= sequence of cycles) throughout the sequence and **3-4** reconstruct treatment lines (= multiple phases).



The work consisted in the comparison of the frequency of chemotherapy sessions with a theoretical regimens of 3 cycles (deemed sufficient to discriminate this protocol) of 21 days with a D0-D7-D21 injections regimen^{3,4}.

Conclusion

This algorithm approximated the number of patients with mTNBC in first line who are treated with the CG protocol in France.

The number of patients benefiting from this protocol and the increase in its use over time are consistent with the data reported by HAS in the efficiency opinion of Keytruda and the recent integration of this therapeutic option into management in France, respectively.

Results

Study Flowchart

Overall, between 2017 and 2020, 21,757 patients were identified as potentially eligible for a CG regimen in metastatic breast cancer patients. ATLAS identified a CG regimen for more than 21 days in 1,358 patients and for more than 42 days in 1,032.

45,715 incidents patients
with metastatic breast cancer

Exclusion criteria  **19,549 patients**
with HER2 + treatment dispensing

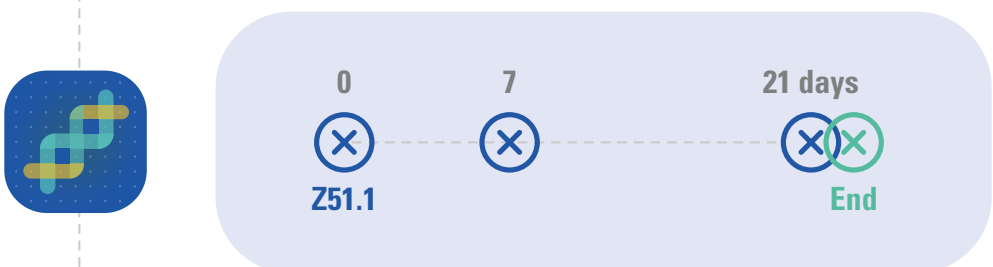
26,166 incidents patients
with metastatic breast cancer

Exclusion criteria  **176 patients**
with CDK4 / 6i treatment dispensing / bilateral oophorectomy

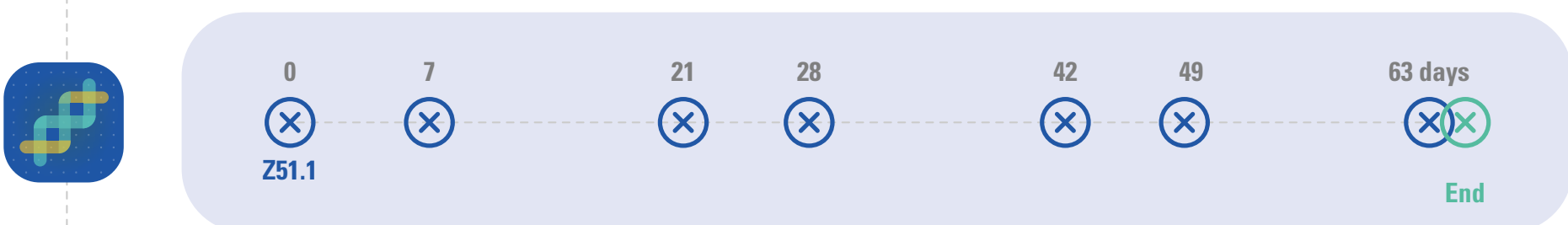
25,990 patients
with metastatic breast cancer (HER2+ patients excluded ; a part of HR+/HER- patients excluded)

Exclusion criteria  **4,233 patients**
with either Bevacizumab / Atezolizumab dispensing or at least two chemotherapy sessions

21,757 patients
ATLAS working database



7,524 patients
with 1 Carbo Gem cycle



2,675 patients
with 3 Carbo Gem cycle

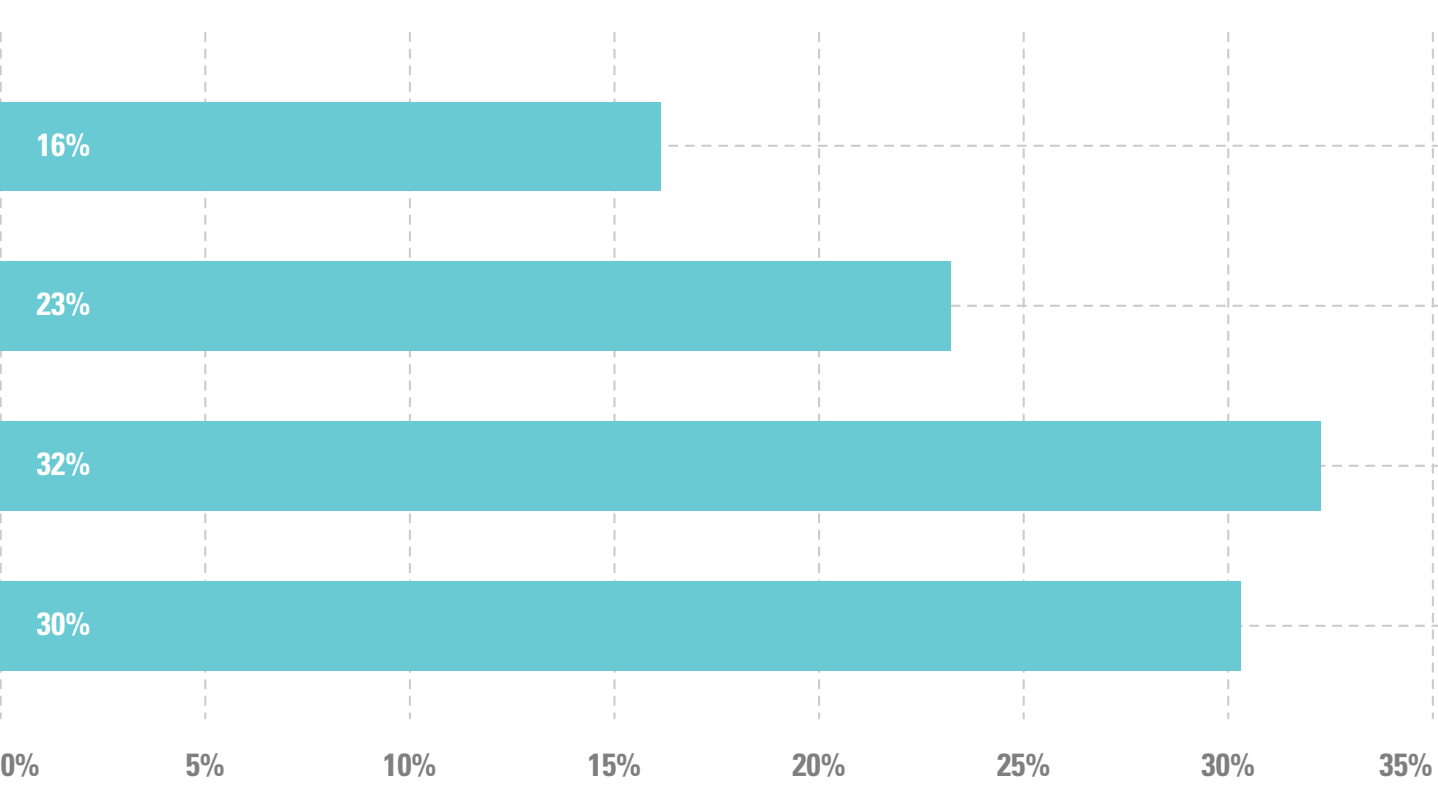
1,358 patients
with Carbo Gem > 21* days

1,032 patients
with Carbo Gem > 42* days

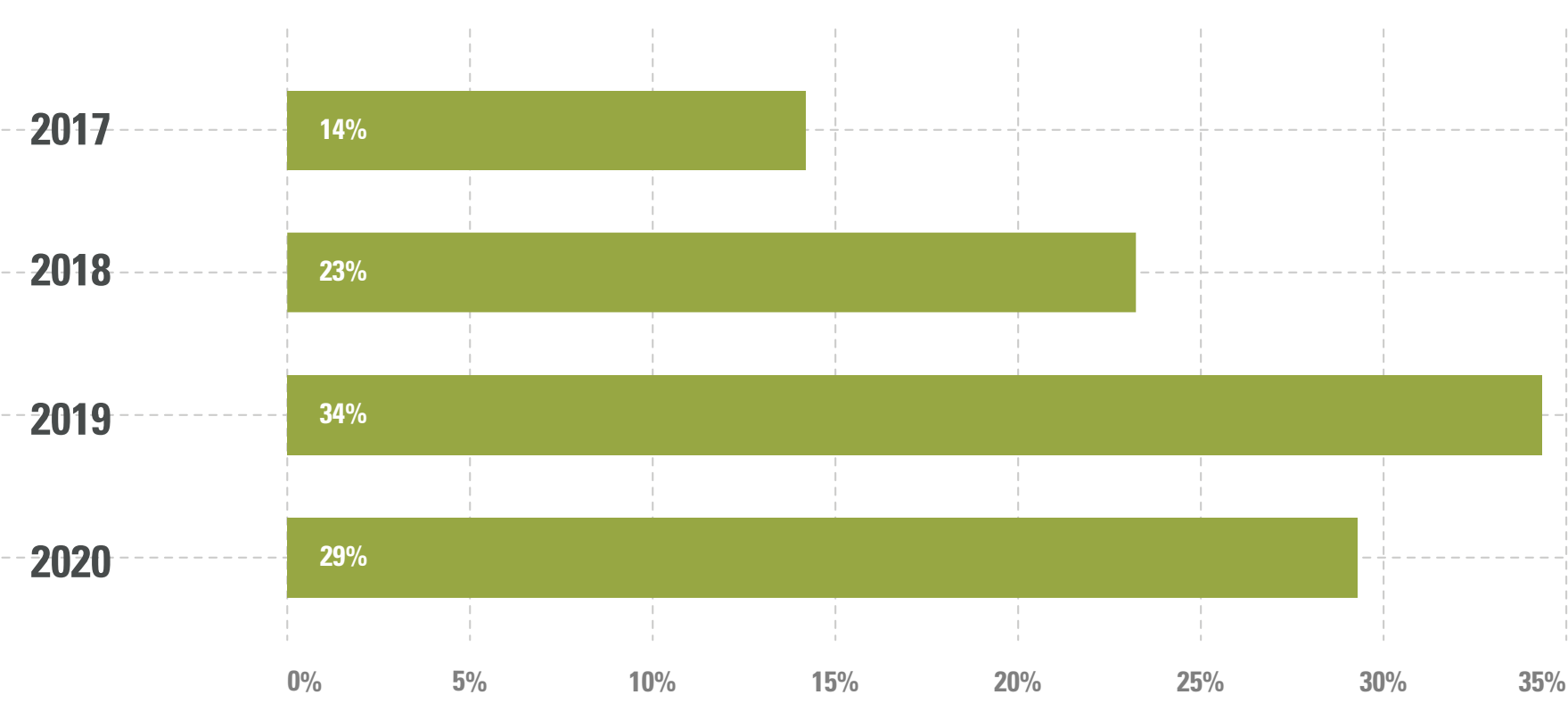
CG regimen distribution among the study years.

Among all CG regimen identified, the increasing tendency started from 14-16% identified in 2017, 23% in 2018, 32-34% in 2019, to 29-30 % in 2020.

Carbo Gem > 21* days



Carbo Gem > 42* days



1. Haute Autorité de Santé. KEYTRUDA (pembrolizumab) - Cancer du sein triple négatif. Saint-Denis La Plaine: HAS; 2022.
2. Cortes J, Rugo HS, Cescon DW, Im SA, Yusuf MM, Gallardo C, et al. Pembrolizumab plus Chemotherapy in Advanced Triple-Negative Breast Cancer. N Engl J Med. 2022 Jul 21;387(3):217–26.
3. Prodel M, Lamarsalle L, Augusto V. ATLAS: A Robust Algorithm for Temporal Sequence Alignment of Treatment Lines using Claim Databases. In: 2019 IEEE Conference on Computational Intelligence in Bioinformatics and Computational Biology (CIBCB). 2019. p. 1–8.
4. Laurent M, Guilmet C, Javelot M, Guigand G, Piérres M, Augusto V, et al. ATLAS – Nouvelle méthode d’analyse des lignes de traitements à partir du système national des données de santé : exemple de l’étude MYLORD, sur les patients français atteints du myélome multiple. Revue d’Épidémiologie et de Santé Publique. 2020 Sep 1;68:S74–5.

PMSI bases provided by ATIH, Data controller: MSD France; Processing implementation officer: Heva. Study registered under MR006 with the Health Data Hub on Nov. 24, 2021 (Declaration of conformity n° 2206271 v 0 of Sept 5, 2018)